REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 14 and 28 are pending in this application. Claim 14 is cancelled and claim 28 is amended herein. No new matter is added.

In support of the remarks and arguments stated *infra*, Applicants have submitted herewith the Declaration of Dr. Dror Harats under 37 C.F.R. §1.132 ("Harats Declaration").

Rejections under 35 U.S.C. §112, first paragraph

Written Description

The Examiner has rejected claims 14 and 28, on page 2 of the Office Action, under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner asserted that there is no support in the specification as originally filed for the recitation of the phrase, "enteric coated composition" suggesting that the specification only supports enteric coated tablets or granules.

Applicants have cancelled claim 14 and amended claim 28 to recite "enteric coated tablet or granule composition". Applicants submit that there is sufficient written description in the specification for claim 28 as amended and request that this rejection be withdrawn.

The Examiner also asserted that there is no support in the instant specification for the phrase "copper oxidized low density lipoprotein" in claims 14 and 28. The Examiner argued that the specification only teaches a particular LDL composition made using specific reagents. The Examiner asserted that the specification does not supply support for any copper oxidized LDL, wherein the term encompasses compositions made using reagents other than copper sulfate at the specific concentrations disclosed in the specification.

Applicants have cancelled claim 14 and amended claim 28 to delete "copper". Applicants submit that there is sufficient written description in the specification for claim 28 as amended and request that this rejection be withdrawn.

The Examiner has rejected claim 14, on page 3 of the Office Action, under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner alleged that claim 14 contains subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the

inventors had possession of the invention when the application was filed. The Examiner alleged that because the instant specification does not provide a listing of the amino acid sequence of all LDL proteins of all animals, that one of ordinary skill in the art would not believe that Applicants had possession of the invention of claim 14.

Applicants have cancelled claim 14. Therefore, this rejection is moot and should be withdrawn.

Enablement

Claims 14 and 28 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Claim 14 has been cancelled. The rejection is traversed with respect to pending claim 28 as amended herein.

The Examiner states that the specification does not disclose how to use the claimed method to treat or prevent atherosclerosis in humans *in vivo* using an oral tolerance inducing amount of oxidized LDL. The Examiner further states that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. *See*, Office Action at pages 6-8.

Applicants submit that pending claim 28 is not directed to the induction of oral tolerance, rather pending claim 28 is directed to a method of treating atherosclerosis by administering a therapeutically effective amount of an enteric coated tablet or granule composition comprising isolated human oxidized LDL and a pharmaceutically acceptable carrier for oral administration, and thus, the Examiner's arguments regarding the unpredictability of disease treatment via inducing oral tolerance to a disease antigen, including the discussion of McKown and Spack *et al.* is improper. In response, the Examiner has stated that although the claims are not directed to a specific mechanism of action, the disclosure indicates that the claimed method works via oral tolerance and that the disclosure is sufficient to maintain the enablement rejection under 35 U.S.C. §112, first paragraph. *See*, Office Action at page 7.

The Examiner's assertion is incorrect. It is well recognized under U.S. law, that it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works. *Newman v. Quigg*, 877 F.2d 1575, 1581 (Fed. Cir. 1989). It is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how the invention works a

necessary element in the specification to satisfy the enablement requirement. *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570 (Fed. Cir. 1983). A patent applicant need only teach how to achieve the claimed result, even if the theory of operation is not correctly explained or even understood. *In re Isaacs,* 347 F.2d 887, 892, 146 USPQ 193, 197 (C.C.P.A. 1965).

Applicants submit that the instant application discloses a method of treating atherosclerosis by administering a therapeutically effective amount of an enteric coated tablet or granule composition comprising isolated human oxidized LDL and a pharmaceutically acceptable carrier for oral administration and thus satisfies the how-to-use requirement of 35 U.S.C. §112, first paragraph, irrespective of whether the claimed method works via oral tolerance or another unidentified mechanism.

The instant invention and the additional data generated using the teachings of the specification and reported in the December 7, 2005 Harats Declaration, readily demonstrate to one of ordinary skill in the art how to make and use the present invention to treat atherosclerosis by oral administration of isolated human oxidized LDL.

Specifically, the instant specification and additional data provides a working example that demonstrates the successful treatment of atherosclerosis in an LDLR deficient mouse by oral administration of isolated human oxidized LDL. *See*, Specification at, *e.g.*, page 15, lines 20-29; and page 18, line 18 to page 19, line 31. It is well recognized in the art that the LDLR deficient mouse is the preferred animal model to evaluate the effects of pharmacologic agents on atherosclerosis. LDLR deficient mice, under appropriate conditions, develop complex atherosclerotic lesions and provide practical atherosclerotic mouse models and are the most utilized model to study lipids and atherosclerosis. *See*, Harats Declaration ¶ 5-6.

As described above, Applicants have provided several working examples and demonstrated successful treatment of atherosclerosis by oral administration of isolated human oxidized LDL. Therefore, Applicants assert that one of ordinary skill in the art, using the teachings of the instant invention would be able to readily determine how to make and use the present invention.

For the above-stated reasons, Applicants submit that amended claim 28 is enabled, and request this rejection be withdrawn.

CONCLUSION

On the basis of the foregoing amendment and remark, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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